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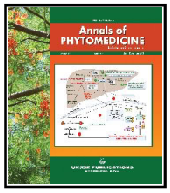

Review Article : Open Access

A comprehensive review of analytical method for ibuprofen by chromatographic technique

P. Shanmugasundaram◆, T. Sudha and K. Sriram

Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Chennai-600117, Tamil Nadu, India

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Abstract

The anti-inflammatory properties of the drug most likely contribute to its analgesic effects. It is a nonsteroidal agent since it prevents the manufacture of prostaglandins and does not affect the adrenal pituitary axis. The pharmacokinetics of ibuprofen are seldom affected by rheumatoid arthritis, advanced age, or the existence of alcoholic liver disease. There is very little ibuprofen in breast milk. Furthermore, the pharmacokinetic profile of acetaminophen and ibuprofen cannot be changed by their combination. Concomitant use of aspirin and ibuprofen; however, appears to lower ibuprofen plasma levels to less than half those observed with ibuprofen alone, this has not yet been clinically proven. The development of ibuprofen was prompted by issues around the use of corticosteroids to treat rheumatoid arthritis, as well as by the established NSAID's general intolerability and gastrointestinal irritation at the time. Unlike the other medications, ibuprofen's therapeutic value was demonstrated to exceed the severity of its adverse effects, which led to its widespread acceptance. The first novel medication to have aspirin's potency without any of its serious side effects was ibuprofen.

1. Introduction

It has been more than since the non-steroidal anti-inflammatory medicine was developed 40 years ago (NSAID), ibuprofen was first prescribed in light of the treatment of arthritic discomfort and swelling and it has been 50 years before the pharmacological effects of the medication were discovered (Adams *et al.,* 1987). The initial guinea pig finding of ibuprofen's anti-inflammatory properties. The UK's Boots Company created ibuprofen in reaction to the requirement for a super aspirin or a safer version of aspirin, free of stomach side effects (Rainsford, 2013). Nonsteroidal anti-inflammatory drugs include ibuprofen and the same class includes aspirin, naproxen (aleve), norboletone (relafen), indomethacin (indocin), and numerous more. These drugs are meant to alleviate inflammation, fever and minor pain. These are brought on through the body's secretion of prostaglandins. The IUPAC names it as (RS)-2-(4-(2-methylpropyl phenyl) propanoic acid. 2-methylpropyl benzene was the first ingredient used in ibuprofen produced originally by the boots group. Cyclooxygenase is inhibited by ibuprofen, an enzymatic that produces prostaglandins, that lowers prostaglandin levels and helps to reduce heat, discomfort and inflammation. The review centers on the diverse chemical and functional characteristics of ibuprofen encompassing experimental investigations and a range of detection techniques including potentiometric, gas chromatography, reverse-HPLC, UV spectrophotometric and high-performance liquid chromatography (Bashyal and Sagar, 2018). NSAIDs, or non-steroidal anti-inflammatory medications, like ibuprofen, are mostly applied locally and taken orally to treat fever and severe pain. This medication's manner of action makes it potentially helpful for treating more chronic illnesses like cystic fibrosis. Because this medication dissolves slowly in aqueous solutions, there is a limit to how quickly it can dissolve in the solid dosage forms that are currently on the market. Because of this, there is a greater chance of unintended side effects following oral administration of high doses due to poor absorption. One issue with the development of injectable solution dosage forms is the poor solubility. Well, it is challenging to create a therapeutic concentration that is effective from topical formulations due to its poor skin permeability (Akella Anuradha *et al.,* 2023). The purpose of this analysis is to offer a summary of the current state of ibuprofen dosage forms, their limitations and the use of particle and crystallization technologies to enhance formulation strategies. It also makes recommendations for ibuprofen's addition to pulmonary medication delivery methods to enhance therapeutic efficacy at low dosages (Irvine *et al.,* 2018).

2. History and discovery

Ibuprofen was first made available to people as an anti-inflammatory medication in England in 1967 and the US in 1974. Milligram for milligram, possesses strong but mild anti-inflammatory qualities comparable to aspirin, but with much less detrimental effects on the stomach. Ibuprofen's history dates back more than 50 years, and it has always been closely associated with our understanding of the inflammatory diseases' pathophysiology mechanisms underlying the medicinal substances. Dr. Stewart Adams is a pharmacologist at the Boots Pure Drug Company in the research division. Nothing was the home company and the main driving force behind the study that ultimately prompted the development of ibuprofen. Nicholson

Corresponding author: Dr. P. Shanmugasundaram

Professor, Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, Tamil nadu, India

E-mail: dean.sps@velsuniv.ac.in

Tel.: +91-9840126575

conducted a thorough analysis of the pharmacological chemistry of propionic acids as well as the process of chemical discovery that led to the creation of ibuprofen. The author highlights the major ideas and significant occasions that led to the development of the most popular NSAIDs, or non-steroidal anti-inflationary. Thompson and Anderson observed that the gastrointestinal blood loss after taking ibuprofen 800-1800 mg/day was comparable to that from placebo or paracetamol (Rainsford and Kim, 2015).

3. Drug profile

Table 1: Drug profile of ibuprofen

Generic name	Ibuprofen
Brand name	Advil, cold and sinus
Type	Small molecule
Molecular formula	$C_{13}H_{18}O_2$
Weight average	206.2808
IUPAC name	Propanoic acid (RS)-2-(4-(2-methyl-propyl) phenyl)

3.1 Structure of ibuprofen

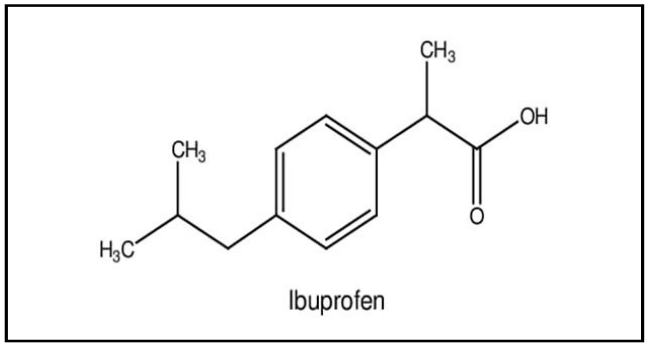

Figure 1: Structure of ibuprofen.

3.2 Physicochemical properties

Density: 1.03 g/cm^3

Melting point: 75-78°C (167-172°F)

Boiling point: 157°C (315°F)

Odor: Distinctive scent

Color: A stable, crystalline solid that lacks color.

3.3 Uses

For the goals of analgesic, antipyretic and anti-inflammatory. Ibuprofen lysine, an ibuprofen salt, is used to treat open ductus arteriosus in the United Kingdom. Because of the lysine salt, ibuprofen is water-soluble in nature. In addition, ibuprofen lysine is used to treat inflammation, fever, and pain. Typically, 200 mg dosages of ibuprofen are sold over the counter in the United States. It can also be obtained with a prescription (Subhamalar *et al.,* 2023; Divya Singh and Sanjeev Singh, 2021).

3.4 Dose

Ibuprofen is available in several forms, including pills and inhalation.

The different dosages based on an individual's age and the type of ailment can be as follows:

- 200-400 mg administered every 4-6 h is used to treat fever and mild pain in patients aged 20-45.
- Three or four times a day, 300-800 mg is used to treat arthritis sufferers.
- Unless on a doctor's prescription, persons should not take ibuprofen for a fever for more than three days or pain relief for longer than ten days.
- Children aged 6 months to 12 years old are frequently given 5-10 mg/kg of ibuprofen every 6-8 h to relieve fever and pain. 40 mg/kg per day is the maximum dosage.
- Treatment for juvenile arthritis involves three to four divided doses of 20-40 mg/kg/day.

3.5 Mechanism of action

Ibuprofen possesses both antipyretic and analgesic qualities. It functions pharmacologically in a manner akin to other standard NSAIDs. Propionic acid is the source of ibuprofen, an NSAID that exhibits aspirin-like cardio protective properties besides having analgesic, antipyretic, and anti-inflammatory qualities. Propionic acid derivatives found in ibuprofen suppress the action of cyclooxygenase I and II, which decreases the production of precursors for thromboxane and prostaglandin. As a result, prostaglandin synthase produces fewer prostaglandins, which is the primary physiological action of the medication. Additionally, ibuprofen reduces the formation of thromboxane A_2 by thromboxane synthase, which prevents platelet aggregation (Law *et al.,* 2014; Himanshu and Priyanka, 2020). When a medication is taken orally, it is quickly and completely absorbed. After being biotransformed into glucuronide conjugate metabolites and expelled in urine, ibuprofen is removed, but not much of the medication remains. Being removed unaltered. Conjugate excretion could be connected to renal function and conjugate buildup takes place in end-stage kidney illness. Cystic fibrosis and hepatic disorders can change the drug's kinetics of disposal. Ibuprofen is not significantly released in quantities found in nursing milk. Important medication combinations that been demonstrated for cholestyramine, acetylsalicylic acid, or aspirin, and metronidazole (Wishart *et al.,* 2018).

Ibuprofen, like other NSAIDs in this class, works by preventing prostaglandin formation, which has analgesic and anti-inflammatory properties. The enzyme cyclo-oxygenase (COX) is the one that NSAIDs inhibit. There are two, the COX enzyme has two isoforms: COX-1 and COX-2. The primary function of COX-1 is prostaglandin synthesis, which is necessary for the maintenance of healthy platelets, kidneys, and gastrointestinal (GI) tract health, among other typical physiological activities (Knox *et al.,* 2011). The process of producing prostaglandins, which are essential for mediating heat, inflammation, and discomfort, is stimulated by COX-2. Nevertheless, it is recognized that in some circumstances, the COX-1 and COX-2 effects could overlap and that the biological impacts of COX-2 activity are significant. Neither COX-1 nor COX-2 is selectively metabolized by ibuprofen. There is little experience using this medication in veterinary medicine and it is approved for use in humans (Rao and Knaus, 2008).

3.6 Indications and clinical uses

The most often prescribed and used NSAID is ibuprofen. It is a very popular over-the-counter drug that is taken for antipyretic, analgesic,

and inflammation relief (Adams *et al.,* 1987). For the management of soft tissue problems, rheumatoid arthritis, osteoarthritis, spondylitis, headaches, migraines and mild to moderate discomfort brought on by dysmenorrhea, ibuprofen and its enantiomer dex-ibuprofen in a racemic combination is frequently used (Potthast *et al.,* 2005). Prolonged gestation and labor, suppression of prostaglandin and thromboxane synthesis and altered platelet function have all been associated with ibuprofen.

3.7 Adverse reaction and side effects

Dogs have been known to vomit and have serious GI ulcers and hemorrhages. Ibuprofen has been linked like other NSAIDs, to renal damage brought on by a reduction in renal perfusion. Animal platelets may be inhibited by ibuprofen (Nivetha *et al.,* 2023).

3.8 Contraindications and precautions

There are no known safe dosages for cats or dogs. Give not to animals that are prone to gastric ulcers. Do not use it with other medications that cause ulcers, such as corticosteroids (Varuni *et al.,* 2023).

3.9 Drug interactions

Reports of specific medication interactions are made. Corticosteroids, however, increase the ulcerogenic effects of NSAIDs, much like they do with other NSAIDs. Ibuprofen and other NSAIDs have the potential to obstruct the effects of diuretics, including furosemide and ACE inhibitors (Dhritimoni and Sumithra, 2023).

3.10 Toxicokinetics

After consumption, ibuprofen is quickly absorbed, taking 1-2 h to reach peak plasma concentrations. When used therapeutically, ibuprofen only makes up a small portion of the overall number of drug-binding sites due to its high protein binding (99%). The distribution volume is between 0.1 and 0.2 litres per kilogram. Ibuprofen enters synovial gaps gradually and stays there in greater amounts as plasma concentrations fall. Ibuprofen crosses the placenta easily (Eraga Sylvester Okhuelegbe, 2020). After being digested extensively, ibuprofen forms four urine metabolites through the process of hydroxylation. Ibuprofen excretes quickly and completely. Ibuprofen elimination has a half-life of 1-2 h. 90% of a dose is eliminated in the urine as inactive metabolites or their conjugates, with the remaining 10% being eliminated as a free drug (Smolinske *et al.,* 1986).

3.11 Toxicity

The exact mechanism of action of ibuprofen is unknown. On the other hand, ibuprofen is categorized as an NSAID and as such it is a non-selective inhibitor of cyclooxygenase, an enzyme that uses the arachidonic acid pathway to produce prostaglandins, which mediate pain and fever and thromboxane which stimulates blood clotting (Bushra and Aslam, 2010).

4. Ibuprofen method development and optimization

Sarowar Jahan *et al*. (2013), the technique was verified in terms of accuracy, precision, specificity, linearity, robustness, sensitivity, and system appropriateness by United States Pharmacopeia (USP) guidelines. ICH states that forced degradation was validated. The method's main purpose was to assay tablets or capsules containing ibuprofen and paracetamol. Additionally, this HPLC approach was used to detect and quantitatively quantify the ingredients in ibuprofen and paracetamol degradation under a variety of conditions, including acidic, alkaline, oxidizing, reducing, and hydrolyzing water. Thus, the information gathered will aid in the development of pharmaceuticals in fields like formulation creation, production and packing in which an understanding of chemical actions can enhance the caliber of pharmaceutical products**.**

Sivakumar *et al*. (2022), one of the most labor-intensive processes in the pharmaceutical business, drying is a necessary step in the production of medicinal powders. The primary goals of the drying process are to increase the stability, solubility and dissolution of pharmaceutical goods to create pharmaceuticals that are like being in a dry condition. While a vast body of research exists on drying processes, little is known about how drying might be applied to process scale-up and drug delivery. The various spray, freeze, and spray-freeze drying particle engineering technologies are embodied in the current communication. Additionally, a brief presentation was given on the production of inhalable powders and possible applications of drying in flavor masking.

Eraga Sylvester (2020) to look at 10 different brands of 400 mg ibuprofen pills that were bought from pharmacies in Benin city, Nigeria, in terms of their pharmacological equivalency. The drug samples were tested for uniformity of weight, friability, melting point, crushing strength, disintegration, and dissolution by recognized and official methods. Using UV and high-performance liquid chromatography, the amount of ibuprofen was found. The medication samples had crushing strengths ranging from 6 to 16 kilopascals and disintegration periods of 7.43 to 10.40 min for uncoated tablets and 3.25 to 37.32 min for coated tablets. The samples' recrystallized ibuprofen had melting points ranging from 73.5 to 76.0°C and their friability values were less than 1%. Two products failed the UV technique of assay for active component content, whereas all brands passed the HPLC test. The amount of ibuprofen released in one hour varied from 18% to 102%. The pharmaceutical grade of ibuprofen (400 mg) pills sold in Benin City, nigeria.

Mounika and Hymavathi (2021), enhancing the ibuprofen's solubility was the primary goal of this study which also aimed to create and verify an analytical technique for figuring out pharmaceuticals in bulk and dose forms for quality control, bioavailability, pharmacokinetic studies and other purposes. The solubility of ibuprofen in aqueous solutions has been greatly enhanced by the use of hydrotropic agents such as sodium benzoate and sodium citrate making it possible to analyze its spectroscopic properties with simplicity and accuracy. The developed method showed remarkable linearity over the concentration range of 10-50 ìg/ml, with a correlation coefficient (R^2) of 0.998. For both hydrotropic agents, the percentage recovery of ibuprofen was found to be almost 100%. The technique was verified for several characteristics, such as precision, accuracy, specificity, and robustness, by the ICH recommendations. The validation trials yielded findings that fell within acceptable bounds, demonstrating the accuracy and dependability of the method for estimating ibuprofen. In summary, the approach developed utilizing the hydrotropic solubilization process offers a quick, easy, and economical means of spectroscopically estimating the amount of ibuprofen present in pharmaceutical formulations. The technique is simple to apply in standard quality control labs for the highly accurate and precise analysis of ibuprofen.

Zunsheng Han *et al.* (2017) ibuprofen and 17 associated substances (chemical process impurities and degradation products) were determined simultaneously using a reversed-phase high-performance liquid chromatography (RP-HPLC) method that was developed and validated. Ibuprofen-containing substance quality control may employ this technique. A variety of chromatographic parameters were assessed, including pH, buffer solution, gradient elution, temperature, wavelength, flow rate, and column. Based on its robustness and separation efficiency, an agilent ZORBAX eclipse plus C18 (250 × 4.6 mm, 5 µm particle size) column at 40°C was chosen. Using acetonitrile as mobile phase B and 10 mm sodium phosphate buffer at pH 6.9 as mobile phase A, the column was eluted at 1.0 ml/min using a gradient. The wavelength of the UV detector was set to 214 nm. In compliance with the requirements of the international conference on harmonization (ICH), this technique was validated to verify its applicability for the system, specificity, linearity, precision, accuracy, sensitivity, robustness, and stability of the sample. This technique was used to examine seven lots of ibuprofen medication goods from various producers.

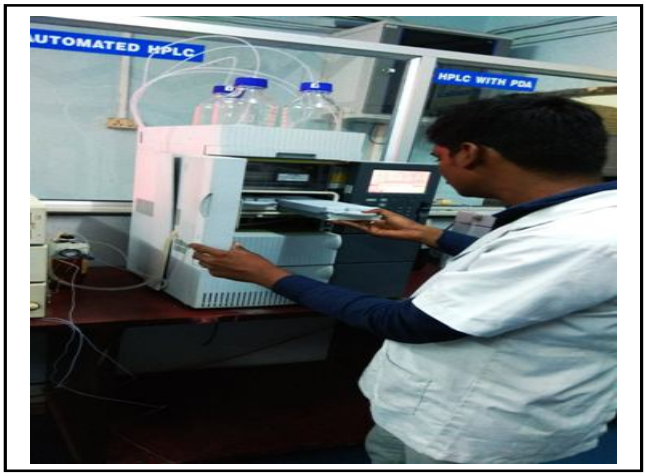

Figure 2: High-performance liquid chromatography.

5. Conclusion

The pain research examined the tolerability of paracetamol, aspirin, and ibuprofen and, the tolerability of over-the-counter (OTC) pain relievers for common, acute discomfort conditions observed in the neighborhood in a blinded, randomized manner. For one to seven days, 8,677 people were randomly assigned to receive treatment with either 1200 mg of ibuprofen, 3 g of paracetamol, or 3 g of aspirin each day. Musculoskeletal disorders headaches (10-11%), sore throats (11-12%), backaches (15-17%), colds or the flu (19-20%) and headaches (31-33%) were the most prevalent reasons for therapy. This meta-analysis, which included 19 trials and 241,138 participants, found that ibuprofen was related to lower temperature at less than 4 h, lower pain at 4 to 24 h and less duration of symptoms than acetaminophen. Unfavorable incidents were rare.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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